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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/674,750	09/30/2003	Vitaly J. Vodyanoy	035721/267665	4229

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EXAMINER	
MONDESI, ROBERT B	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/674,750	VODYANOY ET AL.	
	Examiner	Art Unit	
	Robert B. Mondesi	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 September 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

Claims 1-14 have been canceled. **Claims 21-31** have been added. **Claims 15-31** are pending.

Withdrawal of Objections and Rejections

The rejection of **claims 1-3 and 5-13** under 35 U.S.C § 112 first paragraph is withdrawn.

Maintenance of rejection(s) and objection(s)

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The disclosure remains objected to because even though the following trademarks MILLIPORE (Page 16, Line 3), BIO-RAD, SIGMA (Page 19, Line 3), DNEASY TISSUE KIT (Page 20, Line 20), QUANTINATION REAGENT (Page 20, Line 19), OLYMPUS (Page 22, Line 1), CCD VIDEO CAMERA SYSTEM (Page 22, Line 4), PIERCE SLIDE-A-LAZER 10K (Page 22, line 20), READY GEL (Page 23, Line 3), ATCC (PAGE 26, Line 18) SIGMA, HYCLONE (Page 26, LINE 19), BIORAD (Page 27, Line 9) and ELISA (Page 32, Line 19) have been capitalized, they appear not to be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks. Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 1-3 and 5-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of cyclic amplification of proteons, in a plasma sample, comprising six cycles of incubation for 15 minutes at 60° C, does not reasonably provide enablement for a method of cyclic amplification of proteons in a biological sample involving steps 1a), 1b), 1c), 2a), 2b), 2c), and 2d). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use and make the invention commensurate in scope with these claims.

This rejection was explained in the previous office action.

Claim Rejections - 35 USC § 102

Claims 15-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Bush et al. (cited in the IDS filed February 14, 2004).

This rejection was explained in the previous Office action.

Claims 15 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Campbell et al. (cited in the IDS filed February 14, 2004).

This rejection was explained in the previous Office action.

Response to applicant's arguments

Applicants Urge that the methods as described in the specification generally require that one heat and apply pressure to a sample and thus the art is very predictable, alternatively if the Office action is asserting that such methods of applying heat and pressure are unlikely to create proteons, then the objective truth of the claimed methods is being questioned, and the U.S.P.T.O will be required to explain why the truth or the accuracy of such claims should be doubted.

The applicants assert that a lack of prior published work in an art neither supports or rejects the notion of underlying predictability of the prior art itself. It simply demonstrates the novelty and the non-obviousness of the applicants' invention. In fact, the lack of publication demonstrates that there is no evidence that could be asserted to rebut the presumption of enablement.

In response the examiner would like to state the issue at hand is the breath of the claims in light of the predictability of the art as determined by the number of the working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of recorded. This make and test position is inconsistent with the decisions of *In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)* where it is stated that " ... scope of the claims must bear a reasonable correlation to scope of enablement provided by the specification to the persons of ordinary skill in the

art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. *See in re Wands , 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).* Therefore absent direction/guidance regarding the method of invention, the cyclic amplification of proteons (misfolded proteins) one skill in the art would not be able to practice the claimed invention commensurate in the scope with the claims. In addition, absent direction/guidance regarding the method for the detection of a disorder one skill in the art would not be able to practice the invention.

Applicants assert that Bush et al. and Campbell et al. do not disclose metal clusters of any kind, such as zinc metal clusters and metal clusters are known in the art to be aggregates of two or more atoms bonded to each other by sharing valence electrons and therefore these clusters cannot comprise ions.

Examiner is presently providing a reference that clearly discloses metal clusters bound to proteins comprising metal ions. Otvos et al. 1980, on page 7097, column 1, lines 11-19 ; lines 24-28; lines and figure 3., disclose metal clusters comprising Zn and Cd ions. Otvos et al. teach that having established that the seven metal ions in rabbit liver metallothionein are arranged in such a way as to from separate three-metal and four-metal clusters, it was of considerable interest to attempt to formulate structures consistent with the homonuclear decoupling data (page 7097, column 1, lines 62-65).

New rejection(s) and objections

Drawings

The description of each drawing needs to be an independent sentence that begins with the appropriate numerical and/or alphabetical designation for example. The description of Figure 4b can not begin the middle of a sentence that began with the description of Figure 4a. A new sentence must be written that begins with the designation Figure 4b, followed by the detailed description of the drawing and ... so on.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 30 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to functional fragments of prion protein, beta protein, immunoglobin light chain, serum amyloid, beta protein, aplolipoprotein and calcitorin and ... . The claims do not require that the polypeptides possess any particular conserved structure, or other distinguishing feature, such as a specific biological activity. Thus, the claims are drawn to a genus of polypeptides that is defined by an

unclear functional relationship to each other and to their fragments. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in the claim that is sufficiently disclosed is a partial structure in the form of a recitation of percent identity. The specification does not identify any particular portion of the structure that must be characteristics of the claimed genus are not described. Accordingly, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the a14 that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed." (See page 1117.) The specification does not it clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116), As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of detecting it. The compound

itself is required. See *Fiers* v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird,* 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF' s were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Therefore the full breadth of the claim meets the written description provision of 35 U. S.C. 112, first paragraph. Applicant is reminded that *Vas-cath* makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision.

Claims 30-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir.1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single,

simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the relative skill of those in the art, (5) the predictability or unpredictability of the art, (6) the amount or direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary. Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where no guidance or working examples are provided in the specification and prior art, whereas the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a correspondingly greater quantum of guidance, predictability and skill in the art to overcome classification as undue experimentation. In Wands, the determination that undue experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the claimed invention. (Wands, 8 USPQ2d 1406). Thus, a combination of factors which, when viewed together, would provide an artisan of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that

experimentation as undue. A combination of Wands factors, which provide a very low likelihood of successfully obtaining the claimed invention with additional experimentation, however, would render the additional experimentation undue.

1.Breadth of the claims.

In regards to the method of the invention and the breadth of the claims the broadest interpretation that applies is a method for the detection of a disorder comprising; a)centrifuging a biological sample, b) dividing the supernatant, c) heating a subsample, d) obtaining an aliquot of said heated subsample, e) placing aliquot into an unheated sample, f) heating subsample (e), g) repeating steps d-f and wherein proteons are produced, contacting antibodies that bind to numerous proteins that are indicative of a disorder.

2. The nature of the invention.

The invention is designed to provide is a method for the detection of a disorder comprising; a)centrifuging a biological sample, b) dividing the supernatant, c) heating a subsample, d) obtaining an aliquot of said heated subsample, e) placing aliquot into an unheated sample, f) heating subsample (e), g) repeating steps d-f and wherein proteons are produced, contacting antibodies that bind to numerous proteins that are indicative of a disorder.

3. The state of prior art.

The prior art teaches a method of amplification using cycles of sonication, not heat, to increase the amount of proteons (Soto et al.). Soto et al. teach that specific treatments of a sample containing the prion prominent glyco-protein PrP^C with cycles of

sonication will lead to a conformational change of PrP^{C} to PrP^{Sc} and hence increases the amount of proteons in a plasma sample. The prior art does not discuss a method of detection of a disorder comprising the steps mentioned above

4. The relative skill in the art.

The relative skill in the art as it relates to the administering of therapeutic polypeptides used for the treatment, inhibition, prevention or amelioration of pancreatic disorder is characterized by that of a M.D. or Ph. D. level individual.

5. The level of predictability in the art.

The level of predictability of the method of the invention in the art is low since there is not much known cyclic amplification of proteons using any other method than the method of Soto et al. which uses intervals of sonication and, also since, the prior art does not suggest that any other method can be used to amplify or create preons in order to detect disorders.

6. The amount of guidance present.

The applicants have not provided any guidance or shown to a person skill in the art how the method of the invention can be used to detect disorders.

7. The existence of working examples.

The specification has not provided any examples of a method of detection of disorders. On pages 32-34 the applicants have provided an example of a possible method of detection using antibodies but have not provided any examples of how this method can lead to detection of disorders.

8. The quantity of experimentation necessary.

In the case of a method for the detection of a disorder comprising; a)centrifuging a biological sample, b) dividing the supernatant, c) heating a subsample, d) obtaining an aliquot of said heated subsample, e) placing aliquot into an unheated sample, f) heating subsample (e), g) repeating steps d-f and wherein proteons are produced, contacting antibodies that bind to numerous proteins that are indicative of a disorder more experimentation is required since the applicants have not shown how the method of the invention can be used to detect disorders.

Due to the large quantity of experimentation necessary to provide evidence that the claimed method of invention will detect disorders, the lack of guidance presented in the specification regarding the same, the absence of a working example directed to same, the unpredictable nature of the invention with regards to using proteons to detect, dis orders, the state of the prior art not providing any evidence for any methods od detection using the mentioned steps above, and the breath of the claims which fails to provide particular steps involved in the detection of diordewrs, the specification fails to teach the skilled artisan in the art how to make and use the invention.

Claims 21-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In **claims 21-29** the applicants cite a method of cyclic amplification of proteons involving the multiple cycles of heating; however the applicants have not provided and en result to this method. The applicants need to provide and end point to the method of the invention in claim **21**.

In **claims 22-29**, the applicants cite a method with an unclear end point. The applicants state that the steps are repeated until the number of poteons obtained in each subsample sample is no longer increased; however the applicants have not indicated after how many cycles the number of proteons is no longer increased.

In claims **30-31** the applicants have cited a method comprising steps a-b but without a positive end point. Applicants have not clarified how the multiple heating and centrifuging of samples is supposed to lead to a method of detection.

Conclusion

No claims are allowed

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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